GOLD NANOPARTICLES AND SiRNA COMPLEX FOR TARGETED DRUG DELIVERY

Rupesh Srinivasalu[1], Dr. Isaac Macwan[2], Dr. Prabir Patra[3]
Department of Biomedical Engineering[1,2,3]
University of Bridgeport, Bridgeport, CT

Abstract

This poster is aimed at discussing the various interactions taking place in a SiRNA and gold nanoparticle (SiRNA- AuNp) complex with respect to time. SiRNA are widely used in the field of targeted drug delivery systems due to their higher specificity. The SiRNA-AuNp complex is know to have a higher transfection efficiency compared to that of the traditional methods.

Introduction

Gold nanoparticles have been employed for in vitro, ex vivo and in vivo imaging applications but mainly for serving as scaffolds for therapeutic drug delivery systems. There is a dearth of information intertwined with drug delivery studies particularly the diffusion process through the membrane.

Due to the various federal regulations, these experiments are not directly performed on live subjects and therefore there is a need for simulating the behavior of the processes.

The information derived from the simulations can impact the drug delivery systems in a way that modifications can be done to produce better drug release and better specificity of the intended drug. From various wet lab research it is found that **targeted drug delivery systems (TDDS)** are more effective with the presence of SiRNA and AuNp complex.

SiRNA and Gold Nanoparticle complex

Small interfering RNA (SiRNA) has attracted attention in the field of nucleic acid medicine as a RNA interference (RNAi) application that leads to gene silencing due to specific messenger RNA (mRNA) destruction. However, since SiRNA is unstable in blood and unable to cross the cell membrane, binding/encapsulation of SiRNA into a carrier is required.

Gold nanoparticles serve as an attractive carriers in the targeted drug delivery system (TDDS) due to their functional diversity, cytoxicity, and in vivo excretion properties. There are two ways of assembling SiRNA- AuNp complex covalent attachment and supramolecular assembly. We modeled the complex based on **covalent** assembly with partial **covalent attachment** (~35%) and **electrostatic** (~65%).

Gold nanoparticle in this simulation studies is modeled with a diameter of 8nm in size and the SiRNA are attached to the gold sphere with partial covalent and electrostatic interaction.

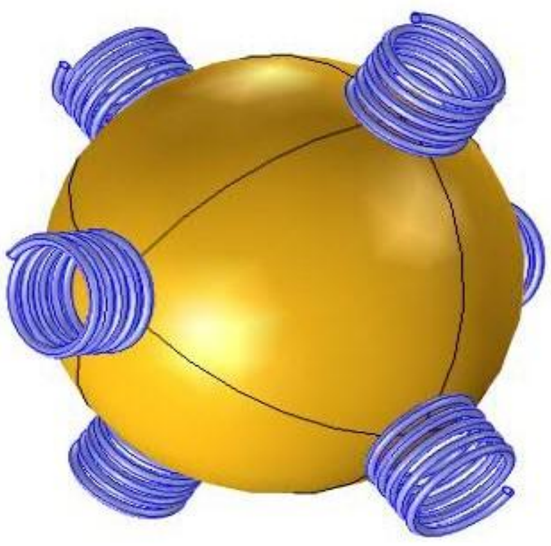

Figure 1: Modeled SiRNA-AuNp complex using COMSOL.

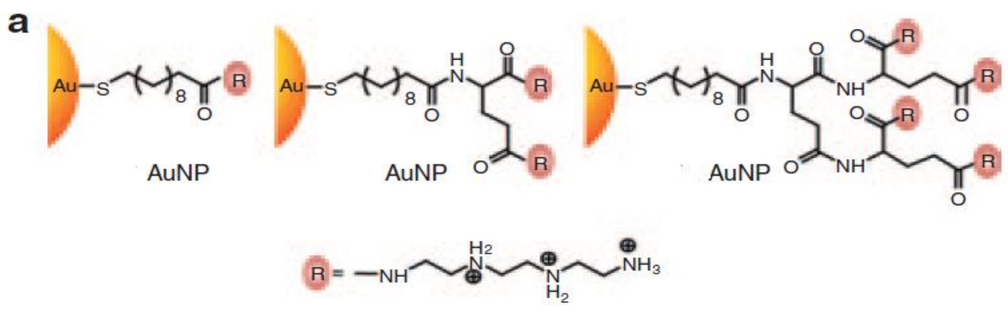

Figure 2: General binding of gold nanoparticles with SiRNA with thiol bond.

Time dependent analysis of SiRNA-AuNp in blood as media.

In Order to examine the stability of the SiRNA- AuNp complex in blood with respect to time as the variable the simulation was performed with defining the medium with the properties of blood with a greater diffusion coefficient.

Under the transport of diluted species module, Time dependent studies was selected after assigning the values of initial concentrations of the species involved the concentration vs time graph was plotted.

Since there are a lot of parameters which play a role in the stability of the complex for example the viscosity, diffusion coefficient, temperature etc., the values which are assigned to these parameters should be as precise and as accurate as possible.

Results

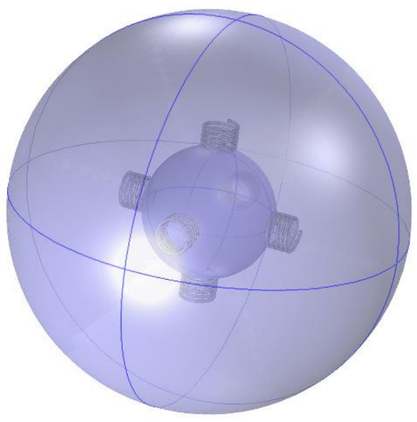

Figure 3: Modeled SiRNA-AuNp encapsulated by a sphere defined with the properties of blood.

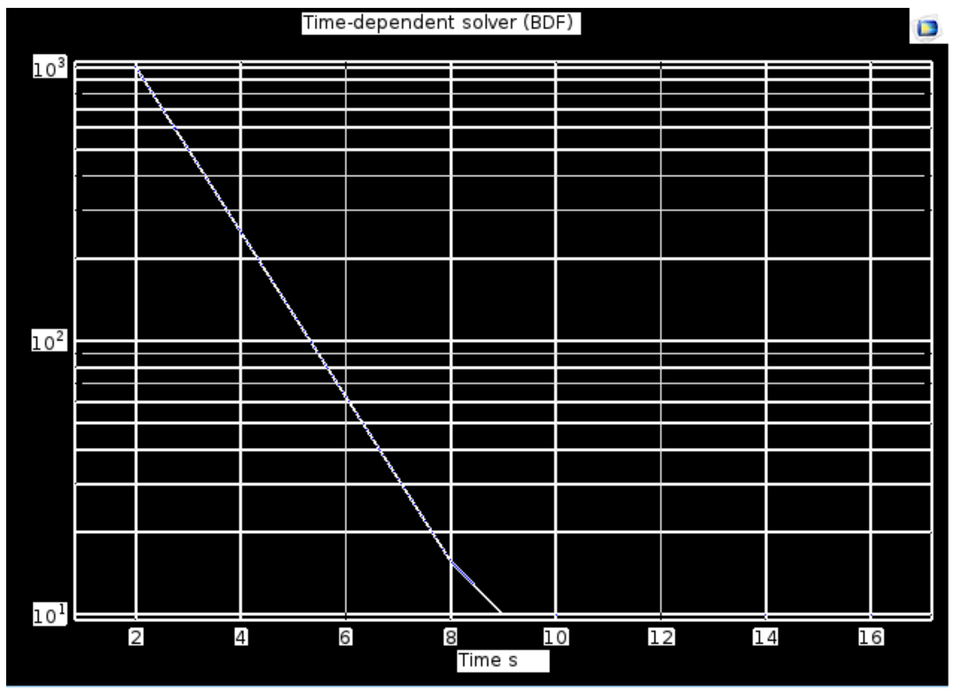

Figure 4: Plot of concentration vs. time graph in blood as media

when plotted with respect to the time shows a steady decrease which is probably the usual case due to the presence of RNAse and other enzymes and proteins which degrade the complex.
However, the presence of gold nanoparticle helps reduce the degradation process when compared to the presence of RNA without gold attached to it.

Conclusion and Future work :

The simulation performed gives data which is convincing and is practically close to that of experimental values. However, further work is being done to study the dynamics of the SiRNA-AuNp complex while diffusing through the membrane. The various parameters which reduce the transfection capability of the complex.
The data generated through the above methods might be instrumental in developing better TDDS. By studying the role of electric field in the drug delivery process it can improve better drug release and also improve the stability of the complex, when the attachment is electrostatic.

References :

1.Nishimura, Y., Mieda, H., Ishii, J., Ogino, C., Fujiwara, T., & Kondo, A. (2013). Targeting cancer cell-specific RNA interference by siRNA delivery using a complex carrier of affibody-displaying bio-nanocapsules and liposomes. [Research Support, Non-U S Gov't]. J Nanobiotechnology, 11(19), 1477-3155.
2. Ding, Ya, Ziwen Jiang, Krishnendu Saha, Chang Soo Kim, Sung Tae Kim, Ryan F. Landis, and Vincent M. Rotello. "Gold nanoparticles for nucleic acid delivery." *Mol. Ther* 22, no. 6 (2014): 1075-1083.